

Amendment to the Claims:

1.-21. (Cancelled)

22. (Currently amended) A method of screening for substances which are capable of inhibiting the phosphorylation of a tau protein by casein kinase 1 (CK1), wherein the tau protein comprises one or more phosphorylation sites, the method comprising:

(a) contacting at least one candidate substance, the tau protein and casein kinase 1 under conditions in which the casein kinase 1 is capable of phosphorylating the site(s) of the tau protein in the absence of the candidate substance;

(b) determining whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of the tau protein at one or more sites of the tau protein by casein kinase 1; and,

(c) selecting the candidate substance which inhibits phosphorylation of the tau protein at one or more of the sites,

wherein the casein kinase 1 phosphorylates tau protein at one or more sites selected from the group consisting of (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 and S435 of tau protein.

23. (Original) The method of claim 22, wherein the casein kinase 1 is a fragment or derivative of full length casein kinase 1 having the amino acid sequence set out between amino acids 1 and 428 inclusive in SEQ ID NO: 1.

24. (Previously presented) The method of claim 22, wherein the casein kinase 1 has greater than 80% sequence identity with full length casein kinase 1 having the amino acid sequence set out between amino acids 1 and 428 inclusive of SEQ ID NO: 1.

25. (Previously presented) The method of claim 22, wherein the nucleic acid molecule encoding the casein kinase 1 is capable of hybridising under stringent conditions to a nucleic acid molecule encoding full length casein kinase 1 having the amino acid sequence set out in SEQ ID NO: 1.

26. (Previously presented) The method of claim 22, wherein the tau protein is paired helical filament tau.
27. (Previously presented) The method of claim 22, wherein the tau protein is a fragment or derivative of full length tau protein having the amino acid sequence set out between amino acids 1 and 441 inclusive in SEQ ID NO: 2
28. (Previously presented) The method of claim 22, wherein the tau protein has greater than 80% sequence identity with full tau protein having the amino acid sequence set out between amino acids 1 and 441 inclusive in SEQ ID NO: 2.
29. (Previously presented) The method of claim 22, wherein a nucleic acid molecule encoding the tau protein is capable of hybridising under stringent conditions to a nucleic acid molecule encoding full length tau protein having the amino acid sequence set out in SEQ ID NO: 3.
30. (Cancelled)
31. (Currently amended) The method of claim ~~30~~22, wherein the sites of the tau protein are selected from S262 and/or S356.
32. (Currently amended) The method of claim ~~30~~22, wherein the sites of the tau protein at one or more sites selected from the group consisting of S113, S258, S289, S416, S433 and S435.
33. (Previously presented) The method of claim 22, wherein the method comprises determining the effect of contacting the candidate substance(s) with a combination of kinases, simultaneously or sequentially applied to the candidate substances and casein kinase 1.
34. (Original) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with one or more of casein kinase 2 (CK2), protein kinase A (PKA), glycogen synthase kinase 3 α (GSK-3 α) or glycogen synthase kinase 3 β (GSK-3 β).

35. (Original) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with PKA and GSK-3 β .
36. (Currently amended) The method of claim 22, wherein the method further comprises determining in step (b) whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of a another substrate by the casein kinase 1.
37. (Cancelled)
38. (Previously presented) The method of claim 36, wherein the method further comprises confirming whether a candidate substance selected in an initial screen has the property of inhibiting the phosphorylation of the tau protein under conditions in which the casein kinase 1 is capable of phosphorylating the site(s) of the tau protein in the absence of the candidate substance.
39. (Previously presented) The method of claim 22, wherein the step of determining the presence, absence or extent of phosphorylation at one or more sites of the tau protein employs mass spectroscopy or a site specific recognition agent which is capable of distinguishing between a phosphorylated and a non-phosphorylated site.
40. (Original) The method of claim 39, wherein the site specific recognition agent is a monoclonal antibody.
41. (Previously presented) The method of claim 22, wherein the screening is carried out in a multiplex assay employing a solid phase on which a plurality of substrates are immobilised.
42. (Original) The method of claim 41, wherein the substrates correspond to phosphorylation sites of tau protein.
43. (Previously presented) The method of claim 22, comprising the further step of optimising the structure of the selected candidate substance.

44. (Currently amended) The method of claim 22 which comprises at least one of the further steps of manufacturing the selected candidate substance and formulating ~~it~~ the selected candidate substance in a pharmaceutical composition.

45. (Previously presented) A method of preparing a pharmaceutical composition or medicament, the method comprising:

- (i) identifying a casein kinase 1 inhibitor according to claim 22;
- (ii) optimising the structure of the casein kinase 1 inhibitor; and
- (iii) preparing the pharmaceutical composition or medicament containing the optimised casein kinase 1 inhibitor.

46. (Previously presented) A substance obtained by the method of claim 22.

47.– 52. (Cancelled)

53. (Previously presented) A method for the treatment of a tauopathy in a patient in need of said treatment, said method comprising administering to said patient a substance obtainable by the method of claim 22.

54. (Currently Amended) The method of claim ~~53~~ 54 wherein the tauopathy is Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, multisystem atrophy (MSA), neurobasal degeneration with iron accumulation, type 1 (Hallervorden-Spatz), argyrophilic grain dementia, Down's syndrome, diffuse neurofibrillary tangles with calcification, dementia pugilistica, Gerstmann-Sträussler-Scheinker disease, myotonic dystrophy, Niemann-Pick disease type C, progressive subcortical gliosis, prion protein cerebral amyloid angiopathy, tangle only dementia, postencephalitic parkinsonism, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, non-Guamanian motor neuron disease with neurofibrillary tangles/dementia, and Parkinson's disease.